

REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-40 were originally filed. Claims 10-18 and 21-40 were withdrawn in response to a restriction requirement. Claims 1-9, 19, and 20 were under examination. Upon entry of the present amendment, claims 5, 6, 9-18, and 21-40 are canceled, whereas claims 7, 8, and 19 are amended. Claims 1-4, 7, 8, 19, and 20 remain pending.

The added recitation of a nucleic acid encoding a polypeptide comprising an amino acid of SEQ ID NO:1 finds support throughout the specification, particularly in claim 2 as originally filed. The added recitation of the complement of a nucleic acid is also supported by the original disclosure in that a nucleic acid is defined as to encompass its single-stranded or double-stranded version, as well as its complementary sequences (*see, e.g.*, page 14 lines 21-23 of the specification). Thus, no new matter is introduced by the present amendment.

II. Claim Rejections

A. 35 U.S.C. §101

The Examiner maintained the rejection of claims 1-9, 19, and 20 under 35 U.S.C. §101 for alleged lack of utility. Applicants respectfully traverse the rejection.

1. Standard to Assess Utility

According to MPEP §2107, the Examiner should review the claims and the supporting written description to determine whether the utility requirement under 35 U.S.C. §101 is met. No rejection based on lack of utility should be made if an invention has a well-established utility, *i.e.*, a utility that will be immediately appreciated by one of ordinary skill in the art based on the characteristics of the invention, regardless any such utility has been asserted. Neither should any rejection be made for lack of utility if an applicant has asserted a specific and substantial utility that would be considered credible by one of ordinary skill in the art.

In most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. MPEP §2107.02 III A. The Court of Customs and Patent Appeals stated in *In re Langer*:

As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of §101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

In re Langer, 183 USPQ 288, at 297 (CCPA, 1974, emphasis in original). To overcome the presumption of sufficient utility as asserted by an applicant, the Examiner must carry the initial burden to make a *prima facie* showing of lack of utility and provide a sufficient evidentiary basis for the conclusion. In other words, the Examiner "must do more than merely question operability--[he] must set forth factual reasons which would lead one skilled in the art to question objective truth of the statement of operability." *In re Gaubert*, 187 USPQ 664, 666 (CCPA 1975).

MPEP §2107.02 IV further states, a detailed explanation should be given for a utility rejection as to why the claimed invention has no specific and substantial asserted utility. Documentary evidence should be provided when possible. Otherwise the Examiner should specifically explain the scientific basis for his factual conclusions.

2. The Asserted Utility Is Specific and Substantial

The present application provides for the first isolation and characterization of human CNG2B, a novel subunit of a cyclic nucleotide gated cation channel. Pending claims are drawn to nucleic acids encoding a CNG2B polypeptide or a subunit of a CNG cation channel. Inventors in this application have specifically asserted that the human CNG2B gene is orthologous to the rat OCNC2 gene and therefore polypeptides encoded by the two genes share the same physiological functions. The rat OCNC2 has been shown to form, with rat OCNC1 alpha subunits, functional heteromultimeric channels involved in olfactory transduction. (*see, e.g.,* bridging paragraph between pages 62 and 63 of the specification). Absent a factual finding to the contrary, as discussed in the last section, the Examiner is thus obligated to accept the inventors' assertion that the novel human CNG2B gene is the ortholog of the rat OCNC2 gene.

Applicants assert that the present invention has a specific utility. A specific utility is defined by the MPEP as a utility that is specific to the subject matter claimed. The MPEP explains that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP §2107.01 and §2107.02. In the present application, Applicants disclose a "disease condition," *i.e.*, altered olfactory signal transduction, that correlates with a "biological activity," *i.e.*, the opening and closing of CNG cation channels. This application provides methods for identifying compounds capable of modulating CNG cation channel activities, which may be used for treating diseases related to abnormal olfactory sensory signal transduction, as well as for assaying scents used in, *e.g.*, food, drug, and cosmetic applications. Applicants thus submit that the present invention has a specific utility, *e.g.*, CNG cation channels can mediate olfactory transduction, which is clearly specific for the cation channels disclosed in the present application and not any ion channels.

Applicants also assert that the present invention has a substantial utility or a "real-world" use. The present invention provides CNG cation channels, discloses that CNG cation channels modulate signal transduction in olfactory, and teaches how to identify modulators of the cation channels. Therefore, there is a real-world use of the invention in the modulation of olfactory sensation, as well as in the identification of compounds that modulate CNG2B channels and thus can be useful as therapeutic agents for treating diseases related to altered olfactory signal transduction, as well as for assaying for novel compounds useful in, *e.g.*, food, drug, and cosmetic applications.

3. The Examiner Has Not Established A Prima Facie Showing of Lack of Utility

The Examiner's rejection of the pending claims for alleged lack of utility was based on the contention that "the instant disclosure fails to provide any experimental data or information on whether the CNG2B protein functions like a cyclic nucleotide-gated cation channel," even though the 93% sequence homology between human CNG2B and rat OCNC2 and their similar expression patterns were acknowledged by the Examiner (bridging paragraph

between pages 3 and 4 of the April 8, 2003, Office Action). It is apparent that the Examiner did not believe the specific and substantial utility asserted by Applicants.

Raising a rejection for lack of utility in such a manner is inconsistent with the proper practice described in the MPEP, which places the initial burden on the Examiner, not Applicants, to provide evidence to support a factual conclusion of the credibility of an asserted utility. In fact, MPEP §2107.02 III.B. specifically cautions Office personnel that, once an assertion of a particular utility is made, "that assertion cannot simply be dismissed as 'wrong,' even when there may be reason to believe the assertion is not entirely accurate." Instead, the Examiner must provide an explanation setting forth the reasoning used in concluding that the asserted specific and substantial utility is not credible; support for factual findings relied upon in reaching the conclusion; and an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. MPEP §2107.02 IV.

The Examiner has not provided a sufficient explanation setting forth the reasoning relied on in concluding that the asserted specific and substantial utility is not credible. The Bork and Koonin reference generally discusses the problems of predicting protein function solely based on a **low level** of sequence homology often limited to **one domain** of a protein. The Examiner attempted to extrapolate from the reference that the human CNG2B as the ortholog of rat OCNC2 would not have the same biological function. Such reasoning is flawed. The danger of erroneously predicting protein function the Bork and Koonin reference has warned against does not specifically apply in the present case where a **high level** of **overall** sequence homology is shown. In the present case, the overall amino acid sequence identity between the human CNG2B polypeptide and the rat OCNC2 protein is greater than 93%. Hence, the Examiner has not offered a valid evidentiary basis for his factual finding that the asserted specific and substantial utility is not credible.

As such, Applicants submit that a *prima facie* showing of lack of utility is not established and the rejection thus cannot properly stand. The withdrawal of the utility rejection is respectfully requested.

B. 35 U.S.C. §112 First Paragraph (Enablement)

The Examiner also maintained the rejection of claims 1-9, 19, and 20 under 35 U.S.C. §112 first paragraph for alleged inadequate enablement. Applicants respectfully traverse the rejection.

Utility-Based Enablement Rejection Is Improper

The Examiner first raised the enablement rejection on the basis that since the claimed invention does not have a well-established utility or a specific and substantial asserted utility, one of ordinary skill in the art would not know how to use the invention. As discussed above, the claimed invention has utility under 35 U.S.C. §101. Applicants thus respectfully request that the enablement rejection on this ground be withdrawn.

The Examiner's Assertion of Lack of Enablement with Regard to the Claim Scope

The Examiner further asserted that the specification does not fully enable one skilled in the art to practice the claimed invention, because the present specification does not provide sufficient guidance on how to make and use the homologues, variants, alleles, and mutants of the CNG2B nucleic acid (page 5 to page 6 of the April 8, 2003, Office Action). Particularly, the Examiner asserted that the functional limitation does not effectively limit the scope of the claimed invention, since the biological activities of CNG2B polypeptides are not established (bridging paragraph between pages 5 and 6). Applicants do not agree with the Examiner's assertions for the reasons that will be specifically discussed below.

The Present Application Is Enabling for Making and Using CNG2B Variants

Contrary to the Examiner's assertion, the present application provides ample guidance for one of skill in the art to make and use the homologues, variants, alleles, and mutants of the CNG2B nucleic acids. For instance, the specification teaches methods for obtaining polynucleotide sequences encoding CNG polypeptides by cloning from cDNA and genomic libraries or by amplification techniques (see page 26 lines 22-30 of the specification). Specifically, the application teaches that a known CNG polynucleotide sequence (such as SEQ ID NO:2 or 3) may be used as a hybridization probe for screening and identifying other CNG2B

nucleic acids (*see, e.g.*, page 26 lines 24-27 of the specification). The specification also discloses primer sequences that can be used to amplify the claimed CNG2B nucleic acids (*see, e.g.*, page 26 line 31 to page 27 line 23; page 28 line 16 to page 29 line 2 of the specification). The specification further teaches that central nervous system (CNS) is a suitable source for isolating CNG2B polynucleotides (*see, e.g.*, page 26 lines 26-27; page 28 lines 3-4). These methods, combined with the knowledge and techniques commonly possessed by one ordinarily skilled artisan, would allow the isolation and acquisition of homologues, variants, alleles, and mutants of the CNG2B nucleic acids through routine experimentation.

The Functional Feature of CNG2B Polypeptides Does Define the Claim Scope

Further contrary to the Examiner's assertion, the functional feature of CNG2B polypeptides does effectively define the scope of the claimed invention. The basis for the Examiner to make such an assertion is the alleged lack of established biological activities of CNG2B polypeptides. The discussions in the earlier sections regarding the utility of the present invention indicate that according to the MPEP and prevailing case law, CNG2B's biological function in olfactory signal transduction as asserted by Applicants is established unless the Examiner can provide a factual finding supported by valid scientific reasoning that such asserted function is not credible.

A functional feature (*e.g.*, characteristic of cyclic nucleotide-gated cation channel) commonly shared by the claimed nucleic acids is readily testable according to the methods disclosed in the present application (*e.g.*, page 42 line 13 to page 50 line 34 of the specification) as well as other methods known to those skilled in the art. Those of ordinary skill in the art would thus be able to rely on these methods to effectively exclude the inoperable embodiments. As such, absent of a *prima facie* showing by the Examiner that the asserted CNG2B's biological function in olfactory signal transduction is not credible, Applicants submit that the functional characteristic recited in pending claims does effectively define the claim scope.

In summary, Applicants believe that the enablement rejection is improperly sustained and respectfully request its withdrawal.

C. 35 U.S.C. §112 First Paragraph (Written description)

The Examiner further maintained the rejection of claims 1, 3, 8, 19, and 20 under 35 U.S.C. §112 first paragraph for alleged inadequate written description. Applicants respectfully traverse the rejection.

The Pending Claims Meet the Lilly Standards

Applicants reiterate that the pending claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, “[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . .” *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description “requires a precise definition, such as by structure, formula, chemical name, or physical properties.” *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Finally, the MPEP states that structural formulas provide a convenient method of demonstrating possession of specific molecules, MPEP 2163.

With regard to the claimed nucleic acids, claims 1 and 8 (and hence claims 3, 19, and 20, which depend from claim 1) set forth both functional elements, *e.g.*, encoding a cyclic nucleotide gated cation channel CNG2B or a subunit of a cation channel, as well as structural elements, *e.g.*, having a certain percentage sequence identity to a reference nucleotide sequence or encoding a polypeptide having a certain percentage sequence identity to a reference amino acid sequence. Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared functional and structural properties.

The nucleotide sequence of a nucleic acid, such as a DNA molecule, is a physical/structural property of the molecule, *see, e.g.*, Stryer, *Biochemistry*, pages 72-73 (3rd ed. 1988), submitted as Exhibit 1 along with Applicants' response filed January 13, 2003. Thus, it is also a physical/structural property of a nucleic acid to have a certain percentage sequence identity to a reference nucleotide sequence, or to encode a polypeptide having an amino acid sequence with a certain percentage sequence identity to a reference amino acid sequence,

because such percentage identity, either in nucleotide sequence or in amino acid sequence of an encoded polypeptide, relies entirely upon the nucleotide sequence of the nucleic acid.

The functional features of the claimed nucleic acids are also provided: each encodes either a CNG2B polypeptide, or a subunit of a cation channel capable of forming, with at least one CNG alpha subunit, a cation channel with CNG characteristics. As required by the standard set forth in *University of California v. Eli Lilly*, these features are common to all members of the claimed genus.

Thus, both structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

The Description of Species Can Properly Support the Description of a Genus

While conceding that proper written description has been provided for nucleic acids of SEQ ID NOs:2 and 3 or a nucleic acid encoding SEQ ID NO:1, the Examiner alleged that the present application does not provide sufficient written description for the homologues, variants, alleles, and mutants of the CNG2B nucleic acid, because there is no disclosure of examples of such homologues, variants, alleles, and mutants (second full paragraph on page 7 of the April 8, 2003, Office Action). Applicants do not agree.

According to the MPEP, there is no need to disclose every species of a claimed genus in order to meet the written description requirement. MPEP §2163 II.A.3.(a) ii) states, "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice." The same section further states that "[w]hat constitutes a 'representative number of species' is an inverse function of the skill and knowledge in the art," and that "there may be situations where one species adequately supports one genus."

In the present case, two representative species (SEQ ID NOs:2 and 3) have been provided as examples of the claimed genus of CNG nucleic acids. Considering the high level of

technical sophistication and the abundance of knowledge in the art of molecular biology and physiology, it would be unfair to require the disclosure of a large number of species to satisfy the written description requirement. Applicants submit that the present application has provided a reasonable "representative number of species" for the claimed genus.

The Asserted Functional Feature Does Describe the Claimed Genus

The Examiner further stated that "the asserted functional limitation, 'encodes either a CNG2B polypeptide, or a subunit of a cation channel capable of forming, with at least one CNG alpha subunit, a cation channel with CNG characteristics,' does not effectively describe the claimed genus," because "the instant disclosure has not disclosed sufficient information on whether the CNG2B polypeptide acts as a cyclic nucleotide-gated channel" (third full paragraph on page 7 of the April 8, 2003, Office Action). Applicants also disagree with the Examiner.

As discussed above in the earlier sections relating to the utility and enablement of the present invention, once Applicants make an assertion regarding the functionality of a claimed invention, the validity and sufficiency of such assertion are presumed. To overcome the presumption, the Examiner must show, by specific evidence and scientific reasoning, why this asserted functionality is not credible. In the present case, the Examiner has not provided such a showing. Thus, the Examiner's reasoning in concluding that the asserted functionality of CNG2B polypeptide does not define the claimed genus of CNG nucleic acids is incorrect and cannot properly serve as the basis of an enablement rejection.

Application of Fiddes v. Baird to the Present Case

In addition, the Examiner cited *Fiddes v. Baird*, 30 USPQ2d 1481 (U.S. Patent and Trademark Office Board of Patent Appeals and Interferences, 1993), to support the position that the instant specification does not properly describe the claimed invention. The Board ruled in *Fiddes* that adequate written description was not present to support a broad claim drawn to mammalian fibroblast growth factors (FGF) when only bovine pituitary FGF amino acid sequence and its theoretical nucleotide sequences were disclosed. Examiner apparently was of the opinion that the facts in *Fiddes* are analogous to that in the present case, such that a finding

of inadequate written description in the present application is warranted. Applicants respectfully disagree with the Examiner's reading of the *Fiddes* case and application of *Fiddes* in the present case.

First, *Fiddes v. Baird* is not inconsistent with the standards for written description as set forth by *Lilly* or *Fiers*. In fact, the Board in *Fiddes* quoted *Fiers* in the discussion of what constitutes adequate written description. 30 USPQ2d at 1483. Moreover, the *Lilly* decision was handed down later in time than *Fiddes* (1997 v. 1993) and by a higher legal authority (Fed. Cir. v. the Board). Thus, even if any inconsistency existed, the *Lilly* decision would be controlling over *Fiddes*.

Second, the fact pattern of *Fiddes* is not analogous to that of the present case. In *Fiddes*, a broad claim was drawn to mammalian FGF based on the specification disclosing a bovine FGF amino acid sequence and a *deduced* nucleotide sequence, but not any actual FGF nucleotide sequence. As it later turned out, the deduced nucleotide sequence disclosed in the specification is significantly different from the actual FGF nucleotide sequence, largely due to codon degeneracy. In essence, the patent applicants in *Fiddes* sought to patent a large genus of polypeptide and polynucleotides when they did not have in their possession any correct polynucleotide sequence. The Board's finding of inadequate written description was based on the notion that the claim of a genus of polynucleotides cannot be adequately supported when only an *inaccurate* polynucleotide sequence was disclosed. The Board in *Fiddes* did not take the position that the claim of a genus cannot be adequately supported by the disclosure of an *accurate* polynucleotide sequence. Nor could the Board, under *Lilly*, properly require the claim of a genus to be supported by the patent applicant's possession of every embodiment of the genus.

In contrast to *Fiddes*, Applicants of the present application have in their possession both the actual nucleotide sequence encoding a CNG subunit (SEQ ID NO:2 or 3) and the amino acid sequence of a CNG subunit (SEQ ID NO:1). In addition, the claims in the present application are not drawn to a broad genus of molecules without specific structural or functional definition (such as a general term of "mammalian CNG nucleic acids"). As discussed

previously, both structural and functional features commonly shared by the claimed genus have been described in detail, which would reasonably convey to the persons of ordinary skill in the art that Applicants had in their possession the claimed invention.

Taken together, the disclosure by the present application provides both the structural/physical features and functional characteristics of the claimed genus of CNG nucleic acids, fully satisfying the written description requirement under *Lilly* and *Fiers*. On the other hand, there exists crucial factual distinction between the present case and *Fiddes v. Baird*, which would make it improper to apply *Fiddes* mechanically. As such, Applicants respectfully request that the Examiner withdraw the rejections.

D. 35 U.S.C. §112 Second Paragraph

Claims 7-9 were rejected under 35 U.S.C. §112 second paragraph for allegedly being indefinite. The Examiner specifically asserted that the phrase "a cyclic nucleotide gated cation channel (CNG) 2B polypeptide" is "determined arbitrarily and may change with time" and therefore renders the claims indefinite. Applicants respectfully traverse the rejection.

According to the MPEP, "applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art." MPEP §2173.01. The term "CNG2B" is defined in the present specification, e.g., on page 10 lines 12-28:

"CNG2B" refers to a polypeptide that is a subunit or monomer of a cyclic nucleotide gated cation channel, and a member of the CNG family. When CNG2B is part of a cation channel, e.g., a homomultimeric or heteromultimeric cation channel, the channel has the characteristic of cyclic nucleotide gating or nitric oxide gating. The term CNG2B therefore refers to CNG2B polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have an amino acid subsequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 95%, 96%, 97%, 98% or 99% or greater amino acid sequence identity, to a CNG2B sequence of SEQ ID NO:1; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence of SEQ ID NO:1 or a fragment or conservatively modified variants thereof; (3)

specifically hybridize under stringent hybridization conditions to a sequence of SEQ ID NOS:2-3 and fragments and conservatively modified variants thereof; (4) have a nucleic acid subsequence that has greater than about 90%, preferably greater than about 96%, 97%, 98%, 99%, or higher nucleotide sequence identity to SEQ ID NO:2 or SEQ ID NO:3; or (5) are amplified by primers that specifically hybridize under stringent hybridization conditions to the same sequence as a primer set selected from the group consisting of SEQ ID NOS:4-13.

Definition for "cyclic nucleotide-gated" or "cyclic nucleotide-gating" is further provided in the specification, *e.g.*, on page 10 line 29 to page 11 line 14:

The phrase "cyclic nucleotide-gated" activity or "cyclic nucleotide-gating" refers to a characteristic of a cation channel composed of individual polypeptide monomers or subunits. Generally, cyclic-nucleotide-gated cation channels are a class of non-selective cation channels that are opened by direct binding of cyclic nucleotides such as cGMP and cAMP. CNG channels are highly permeable to Na⁺ and Ca²⁺, and their activation leads to depolarization and increases in internal Ca²⁺ concentrations. CNG channels can thus link changes in cytoplasmic cyclic nucleotide levels to changes in cellular excitability, secretion of neurotransmitters, and/or stimulation of calcium-dependent pathways. CNG channels play an important role in sensory signal transduction in numerous cells, *e.g.*, cells throughout the central nervous system, in response to primary sensory stimuli such as light and aerosolized or dissolved molecules. In photoreceptor cells, CNG channels are open in darkness due to a high basal concentration of cGMP, causing a tonic depolarization of the membrane and constitutive neurotransmitter release. Upon stimulation by light, cGMP levels drop, closing the CNG channels, and in turn causing a hyperpolarization of the membrane, a drop in the internal Ca²⁺ concentration, and a decrease in neurotransmitter release. CNG channels may also interact with second messenger systems such as the nitric oxide pathway. In some cases, NO may substitute for cyclic nucleotides in gating these channels (see, *e.g.*, Broillet, et al., Neuron 18:951-958 (1997)).

Thus, "CNG2B polypeptide" is a term specifically defined and one of ordinary skill in the art would know the exact metes and bounds of this term upon reading the present disclosure. The Examiner based the indefiniteness rejection on the assertion that CNG2B is an arbitrary name whose meaning may change over time. This is, however, not the standard under 35 U.S.C. §112 first paragraph for an applicant to particularly point out and distinctly claim the invention. As illustrated above, the term "CNG2B" is clearly defined; meanwhile, the Examiner

has not shown that the term as used in pending claims would contradict any currently accepted usage in the art. As such, Applicants submit that the indefiniteness rejection is improper and should be withdrawn.

E. 35 U.S.C. §102(e)

Claims 1, 3, 5-9, 19, and 20 were rejected under 35 U.S.C. §102(e) as the Examiner alleged that they are anticipated by Raumann et al. (WO 02/02633) and Vernet et al. (WO 01/81578). Applicants respectfully traverse the rejections.

The present application claims priority to USSN 60/226,253, filed August 17, 2000. The earliest priority date for the present application is thus **August 17, 2000**. On the other hand, WO 02/02633 was filed June 27, 2001, and published January 10, 2002. Although it claims priority to USSN 60/215,391 (filed June 29, 2000), its 102(e) date is June 27, 2001, and not June 29, 2000, since the priority document USSN 60/215,391 was not published as a U.S. patent application and did not become available to the public until January 10, 2002. Similarly, WO 01/81578 was filed April 26, 2001, and published November 1, 2001. Although it claims priority to USSN 60/201,474 (filed May 3, 2000), its 102(e) date is April 26, 2001. As such, these two references are not available as 102(e) prior art references against the present application. Applicants respectfully request that the anticipation rejections be withdrawn.

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Reply to Office Action of April 8, 2003


PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,


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